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Effectiveness of delivery mode of pharmacist intervention to improve medication adherence and clinical outcomes in people with depression: a systematic review

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ABSTRACT

Depression is a treatable mental health condition with various medication options available. For patients with major depressive disorder (MDD), adherence to antidepressants is essential for effective treatment. However, low medication adherence remains a significant challenge, particularly in individuals with depression. Pharmacists play a crucial role in managing these patients. This systematic review evaluated the impact of pharmacist-led interventions, focusing on the effectiveness of delivery modes (in-person vs. online) in improving medication adherence and clinical outcomes for patients with depression. Randomised and non-randomised controlled trials were included. Data were sourced from PubMed, Scopus, ScienceDirect, and Google Scholar using keywords such as "pharmacist intervention," "education," "medication adherence," "depression," and "medication compliance." Three reviewers independently screened and selected articles, and methodological quality was assessed using the Joanna Briggs Institute Randomized Controlled Trial Checklist. From an initial pool of 791 publications, 364 underwent a comprehensive review, and 14 met the inclusion criteria. The most successful interventions were those conducted face-to-face (83%), compared to those conducted through video and phone calls (16%). However, neither method could improve the severity of depression significantly. Pharmacist interventions can enhance patient adherence to antidepressant medication in patients with depression. Compared to virtual methods, face-to-face techniques are more effective at improving adherence. However, they were not able to improve the symptoms of depression.

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1. INTRODUCTION

Depression is a commonly found mental disorder; around 280 million individuals have been found to have this condition globally [1]. This mental disorder is associated with a lower quality of life, lower functionality, and a higher mortality rate [2]–[4]. Depression is also believed to be a significant issue in public health that is responsible for suicide-related fatality and disability [5], [6]. Regardless of the availability of antidepressants, adults with depression often have low medication adherence, thus challenging their treatment [7]. Many previous studies have revealed that approximately 28% of adults with depression stopped taking their antidepressants [8], [9]. After undergoing treatment for one month, the rate reached 52% after three

months [10]. Another previous study also identified that more than 56% of depressed individuals did not manage to adhere to their treatment plan [11]. Unfortunately, untreated depression can cause relapses of the condition, increase the possibility of emergency department visits and hospitalizations; and lower the response rate to treatment [12]–[15]. Those who are dissatisfied with a treatment plan or experience side effects are more likely to have a higher level of medication non-adherence to antidepressants [16]–[18].

Pharmacists play a crucial role as healthcare providers, helping to improve patients' understanding of the importance of medicines. Pharmacist-led interventions have been shown to contribute to the improvement of adherence and clinical symptoms [19], [20]. However, research has shown different results regarding the effectiveness of pharmacist-led interventions to improve the adherence and clinical symptoms of adults with depression. For example, Rubio-Valera *et al.* [21] found that pharmacist interventions brought significant improvement to adherence to antidepressants. A study by Aljumah and Qureshi [10] also showed that pharmacist interventions improved the adherence of depressed patients from 15 to 27%. The pharmacist interventions responsible for these improvements were in the form of patient advising and supervision [10]. However, there are many other forms of interventions to improve adherence, including monitoring the effects of drugs, helping patients access other treatments, and reminding them of their treatment goals.

However, little research has been conducted on the methods used by pharmacists in assisting adherence programs. Meanwhile, research-based information on various pharmacist-led intervention methods can help design more effective programs to improve adherence. This may be related to the information sources, the communication channel, the optimal setting, the cost of performing the interventions, and its viability in the long run. This necessitates comparing the effectiveness of different methods to design more effective programs. This study aimed to review the results of research on the effectiveness of different pharmacist-led intervention methods on the adherence and clinical symptoms of adults with depression.

2. METHOD

2.1. Strategy of searching and information sources

An extensive literature search was conducted in PubMed, Scopus, and ScienceDirect for publications published from 2003 to 2023. In addition, we searched Google Scholar databases and examined the citations of the included studies. The search approach consisted of combining phrases related to medication adherence in individuals with depression and pharmacies. The keywords used in the study included: pharmacist intervention, pharmacist education, medication adherence, depression, and medication compliance. We also used the terms "OR," "AND," and "NOT" to combine them. MESH was used for the search query in PubMed. Due to the varying limitations and technical differences in the databases, the search methods in both were modified and adapted. We also looked for references from the included articles and Google Scholar to identify other studies that were not included in the systematic search.

2.2. Study selection

The search results were imported and organized using the Mendeley 1.19.8 program. Repetitions were eliminated, and a single author (YF) found publications that may be relevant by reviewing their titles and abstracts. Subsequently, complete texts of articles that may be pertinent were obtained, if they were accessible. A single author (YF) assessed the complete texts to determine their suitability. When uncertainties were detected, two writers (IPS and AWW) separately examined the whole texts to see if they met the criteria for inclusion. In cases where agreement could not be achieved, an additional author (DS and SAK) was engaged, and any differences were addressed through discussion. Relevant studies were defined as those that met the following criteria: being published in the English language, consisting of full-text publications that examined patients with depression, and focusing on the main outcome of adherence to antidepressant drugs. Studies were omitted if the pharmacist did not participate in the intervention or service offered to patients. We omitted many sources of information, including clinical drug trials, conference abstracts, conference reports, systematic reviews, and meta-analyses. Figure 1 displays the PRISMA flow chart illustrating the procedure.

2.3. Quality assessment

The studies included in the analysis were categorized based on their design to facilitate the evaluation of their quality. The Joanna Briggs Institute (JBI) critical assessment techniques [22]–[24] were utilized for all study designs, including randomized controlled trials (RCTs), quasi-experimental, and cohort designs, as shown in Table 1 [25]–[38]. Each question in the JBI checklists was responded to with either a positive affirmation (yes), a negative response (no), an ambiguous answer (unclear or NC), or a statement indicating that the item was not relevant (NA). The number of positive evaluations of the checklists for the assessment tools was used to help determine the quality of the studies featured in the analysis. The ranking for each study was assigned to a low (less than 33%), medium (33-66%), or high quality (over 66%) [39].

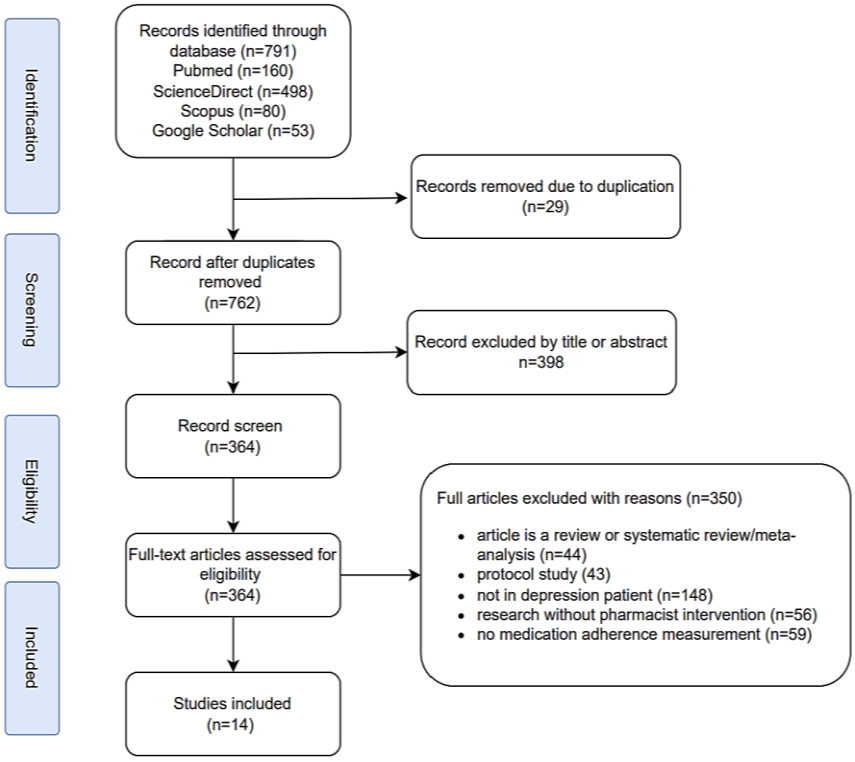

Figure 1. Flow diagram of the selection process of the studies

3. RESULTS AND DISCUSSION

3.1. Included studies and study characteristics

A total of 791 publications were discovered through the literature search, out of which 14 papers fulfilled the inclusion criteria in Figure 1. The study designs were diverse, consisting of 10 randomized controlled trials [25]–[34]. Three researchers utilized an experimental before-and-after design [35]–[37], whereas one study employed a cohort approach [38]. The majority of the studies evaluated were of moderate to high quality. Except for six, the majority of the included RCTs were evaluated as good quality. Out of the three quasi-experimental investigations, two were evaluated as high quality, with scores over 80%. The cohort study, on the other hand, had a quality assessment score of 55%, indicating a medium level of quality. The study's specific attributes are displayed in Table 1. The included studies were performed in various countries, such as the United States of America (USA) (n = 5), Kuwait (n = 1), Australia (n = 1), Saudi Arabia (n = 1), Israel (n = 1), Nigeria (n = 1), Japan (n = 1) and Nepal (n = 1). They were conducted from 2004 to 2023 and were published in English. The studies were conducted in various settings, such as primary care (n = 2), community (n = 5), and outpatient (n = 4). The results and methods of the included studies are presented in Table 1.

3.2. Characteristics of pharmacist intervention

Table 2 (see Appendix) describes the pharmacist's intervention according to the delivery method. This review analyzed the various delivery methods used by pharmacists in their interventions. These include face-to-face meetings (n = 7), phone calls (n = 5), video information (n = 1), and a combination of these methods (n = 1). Besides the study conducted by Brook et al., the other studies included references about the duration of the intervention, which ranged from 2 to 18 months. Out of the total of fourteen studies, eight of the studies were able to show favorable results when pharmacists intervened with patients suffering from depression. A face-to-face approach by a pharmacist is the method that most improves medication adherence in depressed patients.

A telephone call and video information were not effective at improving the adherence of patients with depression to their medication. One study reported that the telephone contact with the patients improved their adherence rate [28]. Another research found that there was no significant improvement in adherence [26], [27], [30], [31], [38]. This lack of change was likely because the control group had a high rate of adherence, and the sample size of the study was too small (n = 60). Nevertheless, the utilization of telephone and video information assistance in clinical practice is constrained due to the constraints of time and expense. Also, patients' level of understanding might be affected by the presence of telephone contact.

The studies encompass a variety of pharmacist interventions. One of the most common interventions that pharmacists provide is education and counselling to help patients adhere to their prescribed antidepressants. Other than this, studies also looked into the effects of medication review [25]–[27], [36]. Some studies also added information leaflets about depression treatment [29]–[34]. Others provided video education [28], [31] phone support [26]–[28], [31], [38], and a cognitive behavior therapy (CBT) program [37]. Counselling and education provided to patients significantly improved their medication adherence. Merely employing a non-face-to-face method to offer counselling and education to patients is insufficient for enhancing medication adherence in individuals with depression.

Table 1. Characteristics of the included articles

Author, year, and country	Study aim	Study design	Sample size, setting	JBI quality percentage (category)
Adler *et al*., 2004, USA [25]	To examine the effect of pharmacist interventions on the mental health of patients with depression in primary care	RCT	533, primary care pharmacy	77% (High)
Capoccia *et al.*, 2004, USA [26]	To examine the effect of pharmacist involvement in collaborative care on improving the quality and outcome of treatment for patients with depression.	RCT	74, primary care pharmacy	46% (Medium)
Rickles *et al*., 2005, USA [27]	To examine the effect of phone-based monitoring and education in collaborative care between pharmacists and patients on the patients' clinical outcomes	RCT	63, community pharmacy	62% (Medium)
Brook *et al*., 2005, USA [28]	To examine the effect of telephone follow-up on patients' willingness to provide feedback to pharmacists and the effect of such feedback on subsequent outcomes.	RCT	60, community pharmacy	38% (Medium)
Saffar *et al.*, 2005, Kuwait [29]	To examine the effectiveness and suitability of two educational interventions on the use of antidepressants in Kuwaiti patients with depression	RCT	270, outpatients	69% (Medium)
Crockett *et al*., 2006, Australia [30]	To examine the effect of rural community pharmacists' responsibilities on the outcomes of patients with depression	Parallel-group design with a control and intervention group	60, community pharmacy	53% (Medium)
Rickles *et al*., 2006, USA [31]	To examine the effect of a telemonitoring tool on patients' willingness to give antidepressant-related feedback to pharmacists and to determine the correlation between patient characteristics and the effect of the feedback on subsequent outcomes	Randomized controlled, experimental design	60, community pharmacy	85% (High)
Aljumah and Hassali, 2015, Saudi Arabia [32]	To examine the effect of SDM-based interventions on the improvement of patients' adherence and outcomes	RCT	239, outpatients	77% (High)
Yusuf *et al*., 2021, Nigeria [33]	To examine the effect of pharmacist interventions on the improvement of adherence to antidepressants	RCT	120, outpatients	77% (High)
Marasine *et al.*, 2022, Nepal [34]	To examine the effect of pharmaceutical services on the adherence and outcomes of patients with depression	RCT	196, outpatients	77% (High)
Desplenter *et al*., 2013, Belgium [35]	To examine the effect of giving comprehensive information to patients on their clinical, economic, and humanistic outcomes	Quasi-experimental design, multi-center, stratified longitudinal	99, outpatients	86% (High)
Klang *et al.*, 2015, Israel [36]	To examine the effectiveness of pharmacist interventions compared to conventional treatment	Nonrandomized, open-label	173, community pharmacy	56% (Medium)
Shoji *et al.*, 2023, Japan [37]	To examine whether using cognitive behavioral therapy (CBT) by community pharmacists is able to improve the adherence and satisfaction of patients with unipolar disorder.	Cluster non-randomized, open-label, parallel-group design	31, community pharmacy	100% (High)
Bhat *et al.*, 2018, USA [38]	To examine the effectiveness of telemonitoring services by clinical pharmacists in collaborative care with a multidisciplinary team	Cohort study	258, outpatients	55% (Medium)

3.3. Medication adherence

The primary outcome of the study was adherence to the use of antidepressant medication. Most studies utilized self-reporting as the primary method of collecting data [26], [29], [30], [32]–[35], [37]. They also gathered information about the individuals' consumption of their medication, such as their medical records or prescriptions [26], [27], [31], [38]. Another study used an electronic pill container [28] and pill counts to verify

the reports [29]. Two studies used morisky medication adherence scale (MMAS) as an instrument to measure adherence to the use of antidepressant medication. Another study utilized the Morisky Green Levine scale and medication adherence rating scale (MARS), while another utilized the antidepressant compliance questionnaire (ADCQ).

Pharmacists play a vital role in helping patients adhere to their prescribed medicine. Eight studies reported that the number of patients who were adhering to their treatment increased. Five studies also found no significant difference between the control and the tested groups, while one study reported no change in adherence rate. The impact of pharmacist intervention on adherence is summarised in Table 2 (see Appendix).

3.4. Clinical outcome

Based on this systematic review, the bulk of the publications examined psychological aspects such as depressive symptoms, satisfaction, knowledge, quality of life, and other related factors. Although some studies reported the median or mean scores of the questionnaires, others noted the percentage of subjects experiencing a significant improvement in their symptoms. Depression symptoms were assessed in ten studies, and out of them, eight studies found no significant disparity in the improvement of depression symptoms between the group that received pharmacist intervention and the control group. Only two studies were able to improve the symptoms of depression using various measures [33], [37]. One study noted that patients' satisfaction with their treatment improved [32], whereas three studies saw an alteration in patients' medication knowledge following pharmacist interaction [27], [29], [31]. Additionally, three studies found no increase in the quality of life for patients with depression [32], [34], [35]. Multiple self-report symptom checklists were utilized in the studies to assess depression symptoms. Specifically, the beck depression inventory (BDI) was employed in several studies [25], [27], [31], [33], the psychological health questionnaire (PHQ-9) was used in two studies [34], [37], the Hopkins symptom checklist (SCL-13) was used in one study [26], the montgomeryeasberg depression rating scale (MADRS) was used in one study [32], and the Kessler psychological distress scale (K10) was used in another study [30]. These studies' results and the measurement of the condition's severity are summarized in Table 2 (see Appendix).

3.5. Discussion

The results of our study indicate that pharmacist-based interventions can improve the adherence of patients with antidepressant medication. Compared to usual care, the interventions were associated with a higher likelihood of patients adhering to their prescriptions. The findings align with the studies conducted by Rubio-Valera *et al.* [21], Aljumah and Hassali [32], and Readdean *et al*. [20], which also shown a favorable impact of pharmacy-based interventions on adherence to antidepressant medication [20], [21], [23]. A total of four studies [33], [35], [37], [38] were not included in the analysis of the study conducted by the three principal investigators: Rubio-Valera *et al.* [21], Aljumah and Hassali [32], and Readdean *et al.* [20].

The evidence shows that the face-to-face mode is an effective pharmacist delivery method in improving adherence in patients with depression. Five studies [25], [29], [34], [36], [40] were successful in improving medication adherence in antidepressant treatment. On the other hand, the results of the phone call intervention and video education were not successful. Only a minority were effective. This study's results differ from previous research, which found that counselling or education through either offline or face-to- face methods was as effective as online or telephone interactions. Various forms of technology can be utilized to help improve the adherence of patients to their medication. Some of these include web-based e-mails, telephone-based assistance, and computer support systems [41], [42]. Other studies also noted that online-based methods were more effective at improving medication adherence than face-to-face ones [43]. A study conducted by Wagner *et al.* [44] found that online-based interventions for depression were just as effective as regular face-to- face therapy. But the long-term efficacy of these methods was only found in the online group [44].

Nevertheless, this study determined that both the face-to-face approach and the telephone technique did not have a substantial effect in enhancing depression symptoms. Most studies discovered similar levels of clinical improvement in both the intervention and usual care cohorts. Only three studies employing the face-to-face technique demonstrated a statistically significant disparity between the two groups throughout the six to eighteen-month follow-up period. This suggests that the pharmacological therapy was successful, but the pharmacist's interventions did not result in significant improvements in depression symptoms. However, other studies did reveal an improvement in patient knowledge and satisfaction with depression therapy. A study revealed that in-person therapy and online cognitive behavioural therapy (e-CBT) were more effective at improving the quality of life for participants with depression. Compared to the e-CBT group, those who took in-person therapy had higher symptomatology scores. Both methods were able to improve the quality of life for the participants, with e-CBT reportedly having a higher rate of participant compliance [45].

Various forms of therapy can be utilized to support individuals dealing with mental health issues. Virtual therapy has gained popularity due to the rise of the COVID-19 pandemic. It provides people with a convenient and comfortable way to connect with a therapist. On the other hand, a therapist's office allows them

to focus on their goals and take a break from their daily lives. There are many advantages to both face-to-face and virtual therapy, and it seems that these will continue to be popular. Non-verbal cues can be used by therapists to help people understand their condition. In-person sessions can provide a deeper understanding of the patient's needs by allowing them to read cues that are not verbal. Nevertheless, the expenses, availability, and scheduling pose as obstacles for face-to-face therapy [46], [47].

Virtual methods, like chatting or sending an email, allow you to keep in touch with a therapist from anywhere. These services make it easy to access therapeutic assistance, and they can be helpful for those who have difficulty traveling to in-person sessions. Virtual interactions can help lower social anxiety when it comes to sharing a physical space with others. Online therapy networks allow individuals to remain anonymous and avoid being seen entering therapy sessions. Some mental health conditions require in-person sessions, and this can be a limitation of online therapy services. Also, individuals who supplement their income through these networks may end up burning out, resulting in inferior care. In addition, the lack of communication between patients and their therapists can limit their understanding [46]–[50].

4. CONCLUSION

This article highlights the fact that pharmacists can have broader responsibilities in patient care through various methods of administering medications, especially concerning the management and medication adherence of adults with depression. This article shows pharmacists performing patient education, medication review, and counselling through face-to-face interactions could effectively improve antidepressant adherence. Therefore, this article provides support for the increasingly significant involvement that |pharmacists may have in both the management of patients with depression and the effort to improve their adherence to therapy.

The study has a limitation that is related to methodological issues. It was quite difficult to assess the findings due to the varying approaches used in the analysis. Although the systematic review identified improved medication adherence, it is ambiguous whether the interventions could also improve depression symptoms. Besides, the included studies employed various methods to measure medication adherence; this shows a lack of standards to measure this phenomenon. These studies also used a limited sample size; thus, a question arises whether or not the findings can be generalized to other populations. It is recommended that future research use larger sample sizes, examine the effectiveness of virtual therapy methods, compare them to conventional face-to-face interventions, and focus on whether or not the interventions could enhance depression symptoms. However, to the best of our knowledge, the findings of this study still offer the first comprehensive analysis of the effects of pharmacist-led intervention methods on the success of the treatment of adults with depression.

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C : **C**onceptualization
M : **M**ethodology
So : **So**ftware
Va : **Va**lidation
Fo : **Fo**rmal analysis
I : **I**nvestigation
R : **R**esources
D : **D**ata Curation
O : Writing - **O**riginal Draft
E : Writing - Review & **E**diting
Vi : **Vi**sualization
Su : **Su**pervision
P : **P**roject administration
Fu : **Fu**nding acquisition

CONFLICT OF INTEREST STATEMENT

Authors state no conflict of interest.

DATA AVAILABILITY

The data that support the findings of this study are available from the corresponding author, [IPS], upon reasonable request.

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APPENDIX

Table 2. Comparison of pharmacist-led intervention delivery modes on medication adherence and secondary outcomes in patients with depression

Author, year	Delivery mode	Intervention description	Duration (month)	Adherence measure	Adherence outcome	Secondary outcome measure	Secondary outcome result
Adler *et al*., 2004 [25]	Face-to-face	Medication review, patient education	18	Self-report: antidepressant (AD) use at 6 months	At 6 months, 57.5% of the intervention group (IG) vs. 46.2% of the control group (CG) were using antidepressants (P = .025)	Depression severity measured by mBDI, mental health index (MHI)-5, mental component summary (MCS), physical component summary (PCS)	mBDI score at 6 months: IG: 17.7, CG: 19.4, P = 0.16 (not significant). MHI-5: 51.9 (IG) vs. 49.0 (CG), P = 0.15. MCS: 40.4 (IG) vs. 38.6 (CG), P = 0.19 PCS: no difference (42.9 for both).
Saffar *et al*., 2005 [29]	Face-to-face	Pharmacist counselling + Arabic leaflet	4-5	Self-report, tablet count	Both interventions improved adherence vs control (P < 0.0005 for the counselling group), with the counselling + leaflet group showing the highest adherence (OR = 5.5, 95% CI: 3.2–9.6).	Clinic attendance, Patient attitudes toward therapy,	Counselling significantly improved clinic attendance compared to control (66% vs 41% at 2 mo; 55% vs 24% at 5 mo) Positive patient attitudes toward treatment were associated with better adherence.
Aljumah and Hassali, 2015 [32]	Face-to-face	Shared decision-making (SDM) education	3-6	Morisky medication adherence scale (MMAS) 8-item version.	After 3 months Vs 5.79 (p = 0.004). After 6 months 4.94 vs 5.99 (p<0.000)	Depression severity measured by the Montgomery–Åsberg depression rating scale (MADRS)	IG showed significant improvement from baseline to 6 months (p < 0.001). However, no significant difference between groups after 6 months (IG: 20.65 vs CG: 20.86, p = 0.897)
Klang *et al*., 2015 [36]	Face-to-face	Medication review + education at enrolment	6	AD use at 6 mo	15.2% vs 55% (*p*<0.0001)	Not reported (NR)	NR
Marasine *et al.*, 2022 [34]	Face-to-face	Educational counselling + leaflet	6	Morisky Green Levine (MGL) scale. Adherence was classified as: high (0 points), medium (1–2 points), and low (3–4 points)	At 2 months: MGL score median (IQR) = 2(2) vs 1(2) (P < .001). At 4 months: MGL score median (IQR) = 2 (1) vs 1(1) (P < .001)	Depression severity is measured using PHQ-9 (Nepali), health-related quality of life (HRQoL) use EQ-5D	No significant improvement in depression or QoL

Table 2. Comparison of pharmacist-led intervention delivery modes on medication adherence and secondary outcomes in patients with depression (continued)

Author, year	Delivery mode	Intervention description	Duration (month)	Adherence measure	Adherence outcome	Secondary outcome measure	Secondary outcome result
Shoji *et al*., 2023 [37]	Face-to-face	CBT-based educational program	11	Drug attitude inventory (DAI)-10	The difference in the change of DAI-10 scores between the groups was statistically significant (p = 0.035)	Depression severity measured by PHQ-9, HRQoL use, EQ-5D-5L (Japanese)	The CBT program successfully improved depression symptoms after 6 months (P = 0.049), but failed to impact quality of life (P = 0.748).
Capoccia *et al.*, 2004 [26]	Phone call	Education, dose adjustment, AE management, follow-up	12	Self-report (days), clinic visits	59% vs 57% There was no significant difference in adherence rates between the IC and CG.	Depression outcomes measured by DSM-IV criteria	No significant difference was found between the IG and CG.
Rickles *et al*., 2005 [27]	Phone call	Monthly calls; assess knowledge, beliefs, side effects	3	Feedback frequency	No difference in adherence; fewer missed doses in the intervention group at 6 months (30% vs 49%).	Depression severity measured by beck depression inventory (BDI)-II, self-report	No effect on depression; improvement in drug knowledge and belief (75% vs 48%)
Brook *et al*. 2005 [28]	Phone call	3 calls + take-home video	6	Electronic pill container	No significant difference (propensity score); per-protocol: 73% vs 90%	Depressive symptoms assessed by change in symptom scores	No significant difference in depression symptoms
Rickles *et al*., 2006 [31]	Phone call	Monthly monitoring & education	6	Pharmacy refill records over 6 months (3 months during the intervention and 3 months post-intervention)	No significant difference in adherence (percentage of missed doses) compared to the CG.	Depression severity measured by BDI-II	No significant difference in BDI-II scores
Crockett *et al.*, 2006 [30]	Video	Pharmacist training via video-conferencing + enhanced counselling	18	Self-report (interview)	95% (CG) vs. 96% (IG); no significant difference between groups, with adherence exceptionally high in both.	Attitude toward medication measured using DAI Psychological well-being: measured using the K10 scale	Psychological Wellbeing, both groups showed significant improvement. Attitude toward medication baseline differences confounded the results; after adjustment, no significant between-group difference remained.
Yusuf *et al*., 2021 [33]	Face-to-face + Phone	One-on-one counselling + monthly phone calls	6	Medication adherence rating scale (MARS)	Significant improvement in adherence was observed at 3 months (P < 0.001) and 6 months (P < 0.001) in the IG.	Depression severity measured by BDI-II[2]	At 6 months, the intervention group had significantly lower depression severity vs. control (17.34 vs. 21.40, P = 0.033).

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